

It is believed that no fee is due; however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason, the Assistant Commissioner is authorized to deduct said fees from deposit account 50-1212/UTXC:504.

Reconsideration of the application is respectfully requested.

### I. AMENDMENT

#### In the Specification

Please insert the following paragraph as the first sentence of the application following the title:

G<sup>1</sup> -- The present application is a continuation of USSN 08/726,211, filed October 4, 1996, now abandoned. --

#### In the Claims

Please amend claims 1, 9, 10, 21, 31, 37 and 52 as follows:

- NE  
CANCELED  
IN  
AMDT/F
1. (Six times amended) A composition comprising a first antisense polynucleotide that hybridizes to a second, Bcl-2-encoding polynucleotide under intracellular conditions and a neutral phospholipid associated with said first polynucleotide, to form a Bcl-2 polynucleotide/neutral phospholipid association, wherein said first polynucleotide comprises at least 8 nucleotides of the sequence CAGCGTGCGCCATCCTTC (SEQ ID NO:1), wherein said polynucleotide is complementary to the translation initiation site of Bcl-2.

- NE  
CANCELED  
IN  
AMDT/F
9. (Five times amended) A composition comprising an expression construct that encodes a first antisense polynucleotide that hybridizes to a second, Bcl-2-encoding polynucleotide

NE  
under intracellular conditions, wherein said construct is under the control of a promoter that is active in eukaryotic cells and associated with a neutral phospholipid, wherein said first polynucleotide comprises at least 8 nucleotides of the sequence CAGCGTGCGCCATCCTTC (SEQ ID NO:1), wherein said polynucleotide is complementary to the translation initiation site of Bcl-2.

- CA  
h2
10. (Twice amended) A method of inhibiting proliferation of a Bcl-2-associated disease cell comprising obtaining a first polynucleotide that hybridizes to a second polynucleotide under intracellular conditions, mixing the first polynucleotide with a neutral phospholipid to form a composition comprising a polynucleotide/phospholipid association, and administering said association to said Bcl-2-associated disease cell to inhibit the proliferation of said disease cell, wherein said cell has a t(14;18) translocation, and wherein the second polynucleotide comprises at least 8 bases of the translation initiation site of Bcl-2 mRNA.

- CB  
h3
21. (Twice amended) A method of inhibiting proliferation of a Bcl-2-associated disease cell having a t(14;18) translocation comprising:
- (a) obtaining an oligonucleotide of from about 8 to about 50 bases and complementary to at least 8 consecutive bases of the translation initiation site of Bcl-2 mRNA;
  - (b) mixing the oligonucleotide with a neutral phospholipid to form a neutral oligonucleotide/phospholipid association; and

GB  
COB+ h3  
conw

- (c) administering said association to said Bcl-2-associated disease cell to inhibit the proliferation of said disease cell.

NE  
CANCELLED  
IN  
AMOT/F

31. (Four times amended) A neutral phospholipid oligonucleotide association comprising a neutral phospholipid associated with an antisense oligonucleotide of from about 8 to about 50 bases and complementary to the translation initiation site of Bcl-2 mRNA, wherein said translation initiation site comprises the sequence CAGCGTGCGCCATCCTTC (SEQ ID NO:1).

NE  
CANCELLED  
IN  
AMOT/F

37. (Twice amended) A composition comprising a neutral phospholipid associated with an expression construct that encodes an oligonucleotide of from about 8 to about 50 bases and complementary to at least 8 bases of the translation initiation site of Bcl-2 mRNA, wherein the construct is under the control of a promoter that is active in eukaryotic cells.

NE  
CANCELLED  
IN  
AMOT/F

52. (Thrice amended) A composition comprising a first antisense polynucleotide that hybridizes to a second, Bcl-2-encoding polynucleotide under intracellular conditions and a primary phosphatide associated with said first polynucleotide, wherein said primary phosphatide is a neutral phospholipid, and wherein said first polynucleotide comprises at least 8 nucleotides of the sequence CAGCGTGCGCCATCCTTC (SEQ ID NO:1), and wherein said polynucleotide is complementary to the translation initiation site of Bcl-2.

Please add the following new claims, claims 57 – 61:

57. The composition of any one of claims 1, 9, 37 or 52, further comprising a charged phospholipid.
58. The composition of claim 57, wherein the charged phospholipid is a positively charged phospholipid.
59. The method of claim 10 or 21, further comprising a charged phospholipid.
60. The method of claim 57, wherein the charged phospholipid is a positively charged phospholipid.
61. The neutral lipid association of claim 31, further comprising positively and negatively charged phospholipids.

---

## **II. REMARKS**

### **A. State of the Claims**

Claims 1, 9, 10, 21, 31, 37 and 52 have been amended. Claims 57-61 have been added.

Claims 1-41, 43-50, 52-61 are currently pending in the case.

Claims 1, 9, 10, 21, 31, 37 and 52 were amended to clarify that the “lipid” contemplated under the claim is specifically a “phospholipid.”